1. **No.**

   FP01906103

2. **Title**

   The Effect of nAChR Signaling on Unfolded Protein Response through IRE1α Activity in Pancreatic β Cells.

3. **Period**

   2018-2020

4. **Summary**

   Secretory cells such as pancreatic β cells are known to be vulnerable to Endoplasmic Reticulum (ER) stress. There are some reports on the Nicotine's cytoprotective effect through the reduction of ER stress in non-pancreatic β cells, but its function in pancreatic β cell is still unknown. In this study, we focused on the ER stress sensor, IRE1α, and aimed to elucidate the role of nAChR signals in the ER stress response mechanism in pancreatic β-cells.

   In rat insulinoma-derived INS1 cells, the ER stress inducer Thapsigargin (Tg) and forced IRE1α activation causes the decrease in Insulin1 mRNA and the increase in the apoptosis precursor TXNIP mRNA. Nicotine attenuated these effects and it also suppressed the increase in IRE1α-specific XBP1 splicing and the phosphorylation of IRE1α.

   We showed that these effects were mediated by nAChR α7 subunit by using siRNA gene knockdown, specific agonist (PNU), and specific inhibitor (αBTX). Furthermore, Nicotine was shown to suppress apoptosis induced by ER stress in the measurement of Caspase 3/7 activity and Annexin V-positive cell rate. In this study, it was suggested that nAChR signal acts on IRE1α and suppresses the ER response via α7 subunit, and finally suppresses apoptosis in pancreatic β cells under ER stress..